

REMARKS

Claims 1, 6-9, 11, 13, 15, 16, 65, 70-80, 90, 95-104, 138, 139, 141 and 143-189 and under examination. Claims 74, 78, 90, 98, 102, 143, 144 and 151 have been amended. Support for the amendments can be found throughout the specification and the claims as filed. In particular, support for the amendment to claims 78, 102 and 151 can be found, for example, on page 31, lines 4-29, which indicates that the ligand on a target can be an antibody. Support for the amendment to claim 143 can be found, for example, in Figures 1 and 2 and on page 3, line 22, to page 4, line 14; page 21, lines 8-29; and page 63, line 12, to page 66, line 15. Accordingly, these amendments do not raise an issue of new matter and entry thereof is respectfully requested.

Rejections Under 35 U.S.C. § 101

The rejection of claims 1, 6-9, 11, 13, 15, 65, 70-79, 90, 95-103, 141, 143-152 and 154-189 under 35 U.S.C. § 101 as allegedly being directed to nonstatutory subject matter is respectfully traversed. Applicants respectfully maintain that the claims are directed to statutory subject matter.

The Office Action refers to the *Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility*, 1300 O.G. 4, November 22. Applicants respectfully point out that MPEP § 2106, "Patent Subject Matter Eligibility," has been revised as of August 2006, and Applicants refer to this revised section of the MPEP for guidance as to the appropriate response to this rejection. First, Applicants respectfully submit that the claims are directed to statutory methods and are not directed to the so-called "judicial exceptions" of an abstract idea, law of nature or natural phenomenon. Even if, *arguendo*, one were to interpret the method claims as relating to an abstract idea, natural phenomenon or a law of nature, MPEP § 2106 IV C indicates that methods and products employing abstract ideas, natural phenomena or laws of nature to perform a real-world function may well be patentable. Claims including excluded subject matter, namely an abstract idea, natural phenomenon or law of nature, are patentable if they are directed to a practical application (MPEP § 2106 IV C 2). MPEP § 2106 further indicates that a claimed invention is directed to a practical application of a 35 U.S.C. §

101 judicial exception when it (A) “transforms” an article or physical object to a different state or thing or (B) otherwise produces a useful, concrete and tangible result.

Even if, *arguendo*, one were to interpret the method claims as relating to an abstract idea, natural phenomenon or a law of nature, Applicants respectfully disagree with the assertion in the Office Action on page 4 that the claimed methods do not recite a “tangible expression.” As indicated in MPEP § 2106, a “tangible result” does not necessarily require that a claim be tied to a particular machine or apparatus or must operate to change articles or materials to a different state or thing (MPEP § 2106 IV C 2 (2) (b)). Rather, the tangible requirement does require that the claim must set forth a “practical application” that produces a “real-world result.” As discussed below in more detail, Applicants respectfully submit that the claimed methods are directed to a useful invention that is practically applied in determining the health state of an individual in comparison to a reference population based on the expression levels of molecules. Accordingly, Applicants respectfully submit that, if the method claims are interpreted to include an abstract idea, natural phenomenon or law of nature, the claims produce a useful, tangible and concrete result.

With regard to claims 141 and 143, Applicants respectfully disagree with the assertion that these claims are not directed to statutory subject matter. MPEP § 2106.01, which relates to computer-related nonstatutory subject matter, indicates that “descriptive material” can be characterized as either “functional descriptive material” or “nonfunctional descriptive material.” “Functional descriptive” material consists of data structures and computer programs which impart functionality when employed as a computer component. “Nonfunctional descriptive material” includes music, literary works and a compilation or mere arrangement of data. Furthermore, “[W]hen functional descriptive material is recorded on some computer-readable medium, it becomes structurally and functionally interrelated to the medium and will be statutory in most cases since use of technology permits the function of the descriptive material to be realized.” Conversely, “[W]hen nonfunctional descriptive material is recorded on some computer-readable medium, in a computer or on an electromagnetic carrier signal, it is not statutory since no requisite functionality is present to satisfy the practical application requirement.” It is clear that the claims are not directed to “nonfunctional descriptive material” such as music, literary works or a compilation or mere arrangement of data.” Accordingly,

Applicants respectfully submit that claim 141, which recites a computer readable medium, should be considered statutory subject matter, as clearly stated in the MPEP.

Regarding claim 143, Applicants respectfully disagree with the assertion in the Office Action on page 4 that “[A] carrier wave is not a physical product and is therefore nonstatutory subject matter.” To the contrary, a carrier wave is an electromagnetic wave and therefore is a physical entity. Furthermore, the MPEP acknowledges that “on some computer-readable medium, in a computer or on an electromagnetic carrier wave” are alternatives for recording descriptive material. In addition, the specification teaches that a computer-readable medium and a carrier wave are alternatives for providing instructions to a processor (page 124, lines 4-18). Accordingly, Applicants respectfully submit that claim 143 is directed to statutory subject matter.

Applicants respectfully submit that claims 1, 6-9, 11, 13, 15, 65, 70-79, 90, 95-103, 141, 143-152 and 154-189 are directed to statutory subject matter. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claims 1, 6-9, 11, 13, 15, 16, 65, 70-80, 90, 95-104, 138, 139, 141 and 143-189 under 35 U.S.C. § 101 and § 112, first paragraph, as allegedly lacking utility is respectfully traversed. Applicants respectfully submit that the claims have utility.

Applicants respectfully disagree with the assertion in the Office Action on page 5 that the disclosed utility is not applicable to the instant claims. To the contrary, the specification teaches, for example, on page 5, line 25, to page 6, line 16, that the methods of the invention can be used in a multiparameter analysis by measuring the expression levels of multiple molecules representative of the health state of an individual. The expression levels of the sample of molecules can be compared to the other molecules of the sample of molecules and to one or more health-associated reference expression regions in a multidimensional analysis. Such a comparison is useful for determining whether an individual has a health state similar to that of the reference population, for example, a healthy individual, or a health state that deviates from the reference population, for example, a disease state.

The specification further teaches, for example, on page 6, line 21, to page 7, line 3, that the methods of the invention are advantageous in that they can be used to predict the health state of an individual by determining whether the individual has a reference expression profile indicative of a reference health state or a perturbed expression profile indicative of a potential disease state in the individual or of a predisposition to developing a disease. The methods of the invention provide a multiparameter analysis of an individual's expression profile by measuring the expression level of multiple molecules, thus allowing the determination of an expression profile that is predictive of an individual's health, including the diagnosis of a disease, the prognosis of a disease, or estimating the course of a disease.

The specification additionally teaches on page 67, line 28, to page 68, line 8, that the methods of the invention are advantageous in that an expression profile can be analyzed to determine the health state of an individual. Such methods are useful for routine health screening to determine if an individual has a reference health state, particularly if the reference individuals are healthy, or perturbed health state that requires further medical analysis or monitoring or that indicates a particular disease or a predisposition to develop a particular disease. The methods of the invention are thus useful in a variety of applications for predictive medicine and preventive medicine.

Applicants respectfully further disagree with the assertion in the Office Action on page 5 that the specification does not disclose any information about "health-associated" reference individuals and/or what a "health-associated" reference indicates. To the contrary, the specification teaches that a "reference individual" refers to an individual selected for comparison using defined criteria and that a "reference population" refers to a group of two or more reference individuals (page 22, lines 8-15). The specification further teaches criteria for the inclusion of an individual as a reference individual including, for example, a healthy individual or an individual having a particular disease, age, gender, ethnic background, drug use, or other criteria useful for comparing the health state of an individual (page 22, lines 16-25; page 70, lines 1-14). Thus, contrary to the assertion in the Office Action, the specification clearly teaches appropriate and sufficient criteria for reference individuals or populations for use in the claimed methods.

Furthermore, Applicants respectfully disagree with the assertion in the Office Action on page 6 that the claimed method does not have a “result” that is “of immediate benefit” because one skilled in the art would not know what a “perturbed” profile indicates. To the contrary, it is clear from the teachings of the specification that a “perturbed expression profile” refers to a characteristic representation of the expression state of a sample of molecules of a population that falls outside a health-associated reference expression region, that is, statistically differs from the reference population (page 28, line 15, to page 29, line 11). Furthermore, such information can be used to determine the health state of an individual, including whether a person has expression levels that fall within those of a reference population, for example, a population of healthy individuals, or outside of the reference population and is in a “perturbed” health state (page 29, line 18, to page 30, line 9). The methods are useful for predictive and preventative medicine and therefore clearly have a specific, substantial and credible utility.

Contrary to the assertion on page 6 with respect to claims 138, 139, 141 and 143, the computer system and computer readable medium for performing steps of the methods of the invention also have a specific, substantial and credible utility, for the reasons discussed above.

Applicants respectfully submit that the claims have a specific, substantial and credible utility. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 112, First Paragraph

The rejection of claims 8, 72 and 96 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement is respectfully traversed. Applicants respectfully submit that the specification provides sufficient description and guidance to enable the claimed methods.

The specification teaches that the methods of the invention can be used to determine the course of a disease (see, for example, page 8, lines 21-29; page 9, lines 13-17; page 11, lines 8-13; page 46, lines 15-26). Furthermore, the specification teaches that the course of a disease includes the stage or severity of the disease, and can include the response of a patient to one or more treatments (page 8, lines 27-29). Applicants respectfully submit that the specification provides sufficient description and guidance to enable a method that indicates the course of a disease. Moreover, the Office Action indicates that “[P]rior art analysis shows that monitoring

the ‘course’ of a disease requires, for example, obtaining a response curve, i.e., measuring gene or protein abundance in cells in response to a treatment (perturbation) over time” (Office Action, paragraph bridging pages 8-9).

As indicated in MPEP § 2164.01, “[T]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.” *United States v. Teletronics, Inc.* 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). Furthermore, the specification need not disclose, and preferably omits, that which is well-known to those skilled and already available to the public. *In re Buchner*, 929 F.2d 660, 661, 18 U.S.P.Q.2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 U.S.P.Q. 481, 489 (Fed. Cir. 1984). Applicants respectfully submit that, based on the teachings in the specification and what was well known in the art, it would be clear to one skilled in the art how to use the claimed methods to determine the course of a disease.

Applicants respectfully submit that the specification provides sufficient description and guidance to enable the claimed methods. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The rejection of claims 8, 72, 74, 78, 96, 98, 102 and 151 under 35 U.S.C. § 112, second paragraph. Applicants respectfully submit that the claims are clear and definite.

In the Office Action, claims 74, 78, 98 and 102 are alleged to be indefinite as being unclear as to whether there is a further limitation to the method steps or the data. Claims 74, 78, 98 and 102 have been amended to recite that the expression levels “of the n molecules” are determined. Applicants respectfully submit that it is clear that the claim further limits how the expression levels of the n molecules are determined, that is, by contacting the specimen with an array or ligands that are antibodies and measuring the expression levels of the n molecules.

Accordingly, Applicants respectfully submit that the claims are clear and definite and request that this rejection be withdrawn.

The Office Action additionally indicates that claims 78, 102 and 151 are allegedly indefinite for the recitation of “antibody ligands.” Although it is respectfully submitted that the meaning of the term “antibody ligands” is clear based on the teachings in the specification, these claims have nevertheless been amended to recite “ligands, wherein said ligands are antibodies,” to more clearly indicate that the ligands are antibodies. Accordingly, Applicants respectfully submit that the claims are clear and definite and request that this rejection be withdrawn.

In the Office Action, claims 90 and 144 are alleged to be indefinite in that it is unclear how the result of the method relates to the preamble and whether the preamble is intended to limit the method claim. These claims have been amended to recite “thereby diagnosing a health state in an individual” to explicitly relate the body of the specification to the preamble. Accordingly, Applicants respectfully submit that the claims are clear and definite and request that this rejection be withdrawn.

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

09/724,898

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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